Armed Forces College of Medicine

AFCM

Diseases of kidney

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Lec (1)
Pathogenesis of Glomerulonephritis &
NephrOtic syndrome

INTENDED LEARNING OBJECTIVES (ILOs)

By the end of this lecture the students will be able to:

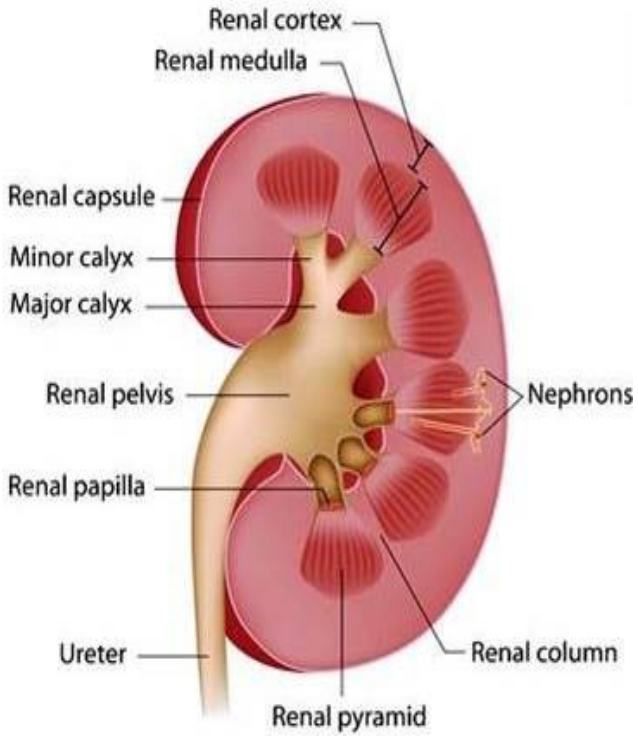
1.Determine the cause of the abnormal findings in blood and urine of nephrotic syndrome cases.

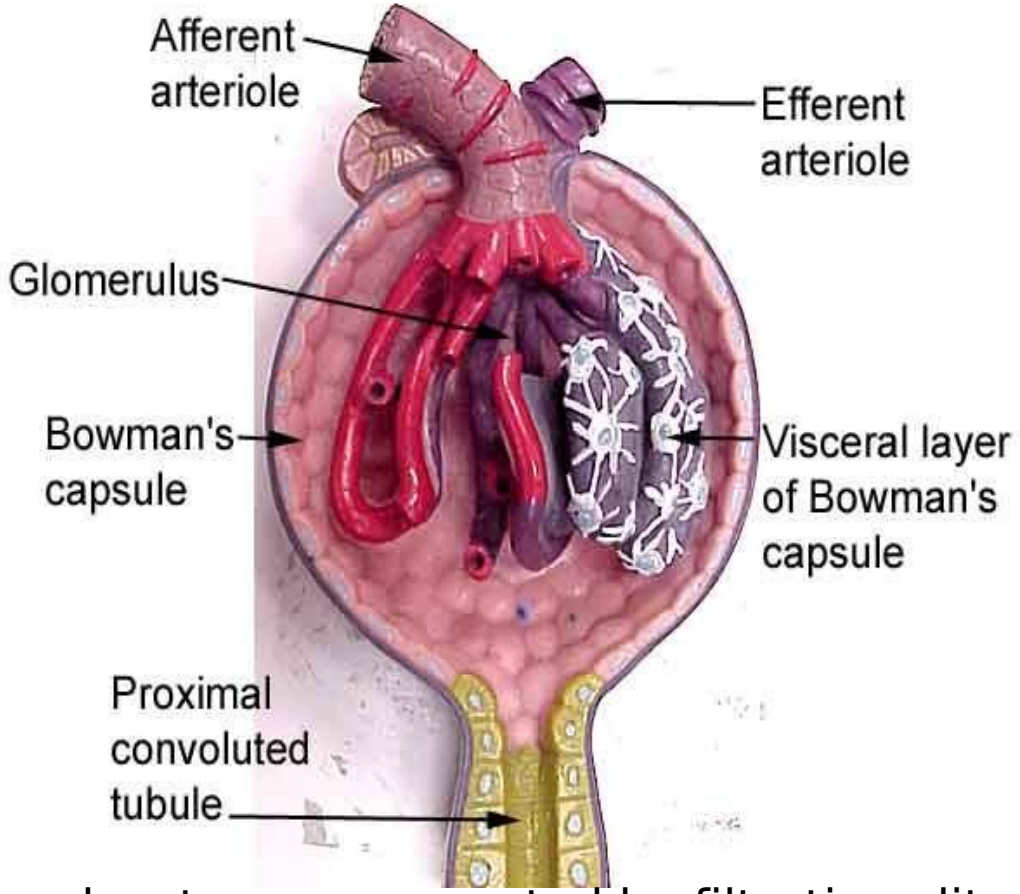
2.List different types of glomerulonephritis causing nephrotic syndrome.

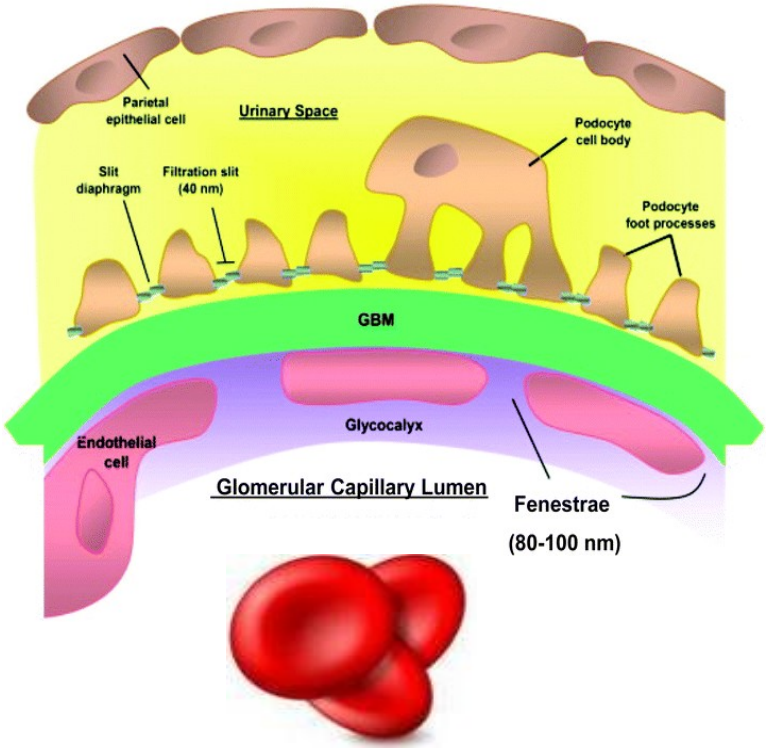
3.Explain the pathogenesis of different types of glomerulonephritis causing nephrotic syndrome.

4.Compare between different types of glomerulonephritis causing nephrotic syndrome regarding their histopathological features

Structure of the glomerulus







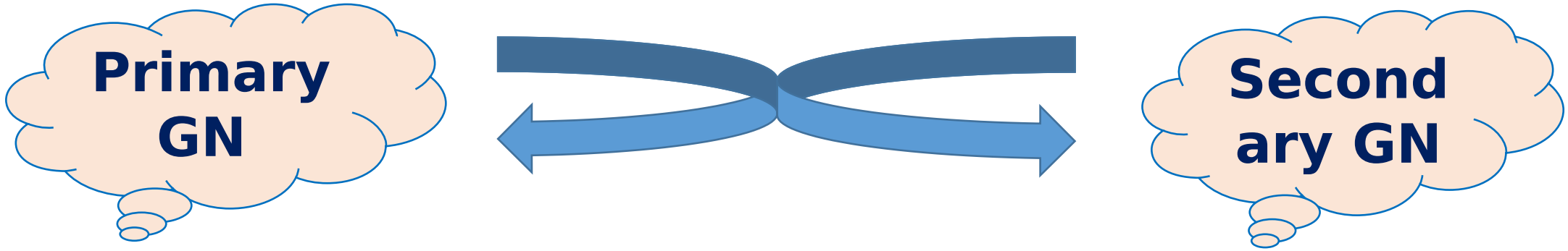
Podocytes

- Foot processes of podocytes are separated by filtration slits that are bridged by a thin slit diaphragm composed of proteins, including podocin, maintaining the selective permeability of the glomerular filtration barrier.
- Podocytes are responsible for synthesis of GBM components.

Glomerulonephritis (GN)

Definition: Diseases involve the **renal glomeruli**.

Types of Glomerulonephritis

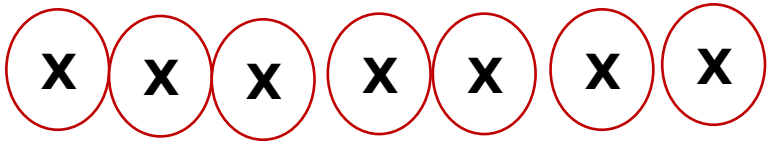


Limited to kidneys

kidneys affected with other parts of the bod

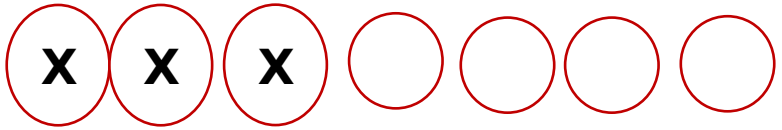
- Systemic lupus erythematosus (SLE)
- Diabetes mellitus
- Hypertension
- Infections e.g. viral B & C hepatitis & Bilharziasis

Histological patterns of glomerular affection



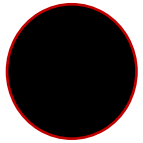
Diffuse

All the glomeruli are affected



Focal

Some glomeruli are affected



Global

The entire glomerulus is affected

Segmental

Only a portion of the glomerulus is affected

Pathogenesis of Glomerulonephritis

A- immune complexes (IC) mediated

Circulating IC	In situ IC
• Antigen–antibody complexes are formed in the circulation and are then trapped in the glomeruli • The antigen is **NOT** of glomerular origin.	• Antibodies deposit in the glomerulus • Antibodies react directly with **1- Glomerular antigen (Non-basement membrane)** **2-Non-glomerular antigens (implanted in glomerulus)**

B- Anti-Glomerular Basement Membrane Antibody-Mediated

C- Activation of alternative complement pathway

D- T cell mediated immune injury

Pathogenesis of Nephrotic syndrome

Nephrotic syndrome

1- Massive proteinuria **3.5 gm or more** protein lost in urine /day

Cause: increased glomerular capillary permeability to plasma proteins due to structural or physiochemical alteration in glomerular basement membrane (GBM) & effacement of foot processes of podocytes

2- Hypoalbuminemia

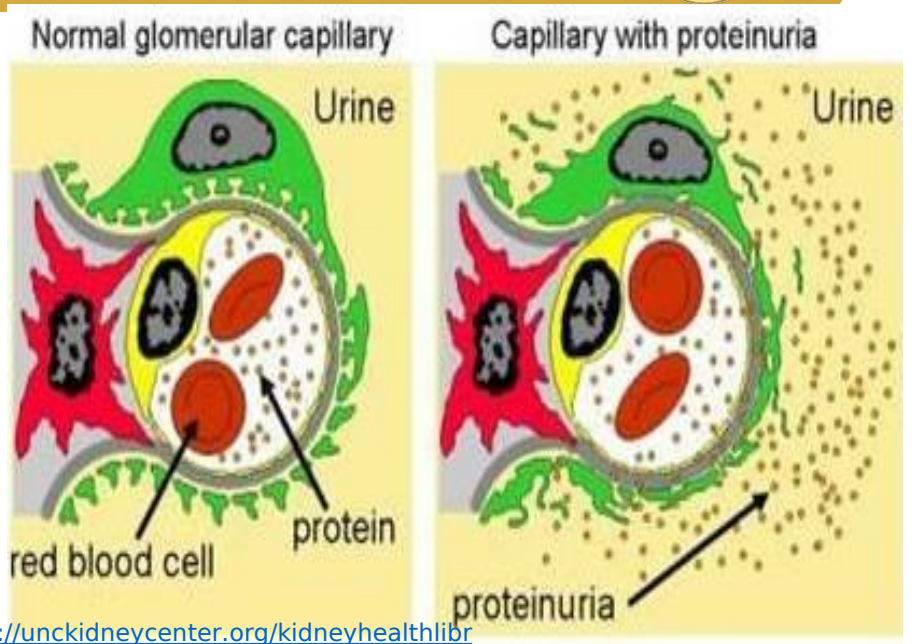
- Plasma albumin levels less than **3 gm/dl**
- Due to heavy proteinuria

3- Generalized oedema

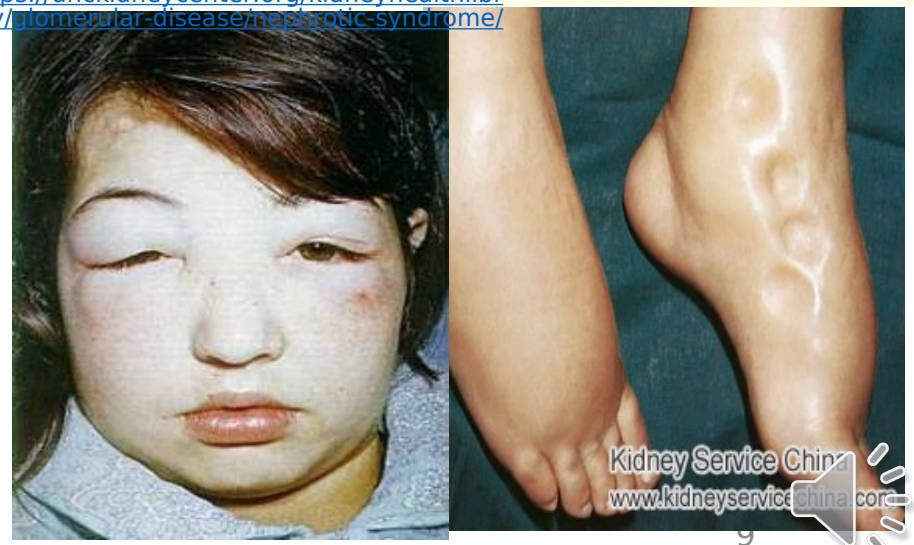
- Due to decreases plasma colloid osmotic pressure → so fluid escapes from the vascular tree into the tissues
- Drop in plasma volume stimulate kidney to release renin → salt water retention aggravating edema

4- Hyperlipidaemia and lipiduria Due to

- Increased synthesis of lipoproteins in liver



https://unckidneycenter.org/kidneyhealthlibrary/glomerular-disease/nephrotic-syndrome/



https://medical-dictionary.thefreedictionary.com/gut+edema

Nephrotic syndrome

Causes of the nephrotic syndrome:

I.Primary glomerulonephritis

1. Minimal change glomerulonephritis
2. Membranous glomerulonephritis
3. Membrano-proliferative glomerulonephritis
4. Focal segmental glomerulosclerois

Described by their histology

II. *Secondary glomerulonephritis due to"systemic diseases" as:*

1. Systemic lupus erythematosus (SLE)
2. Diabetes Mellitus
3. Amyloidosis.

Described by the underlying cause

Have the same histologic patterns as primary

1. Minimal change glomerulonephritis

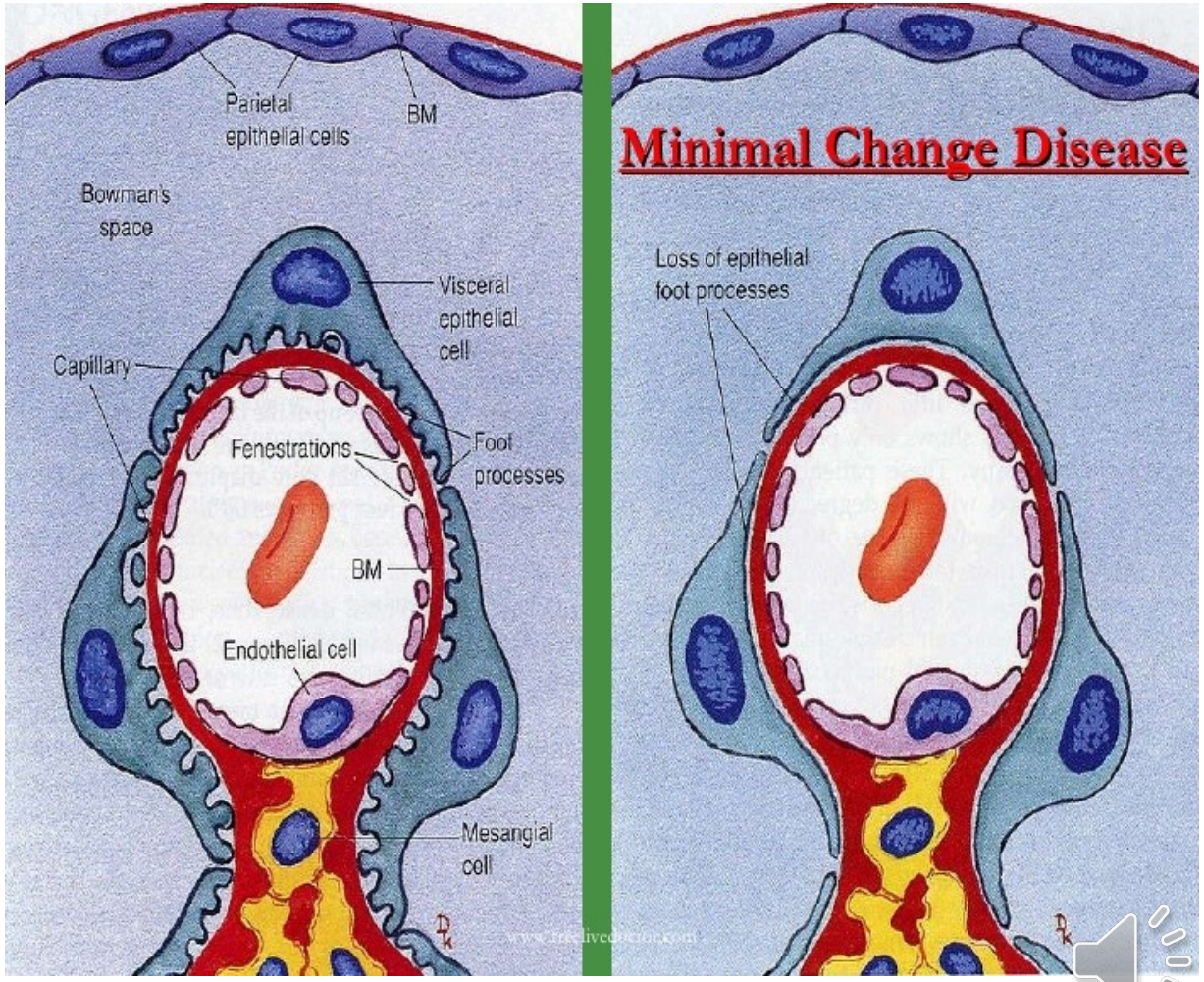
Most frequent cause of nephrotic syndrome in CHILDREN

Pathogenesis:

Circulating **T cell–derived factor** → causes podocyte damage & effacement of foot processes

Mic:

- **Light microscopy: Glomeruli: appear normal**
- **Electron microscopy: *Diffuse effacement*** of foot processes of podocyte
- **Immunofluorescence: Negative findings**



Fate:

- The prognosis is **excellent**.
- Most cases are cured by ***corticosteroid therapy***

2. Membranous glomerulonephritis (MGN)

ADULTS are affected

Pathogenesis:

- **in situ Immune complexes**

Induced by antibodies reacting **in situ** to

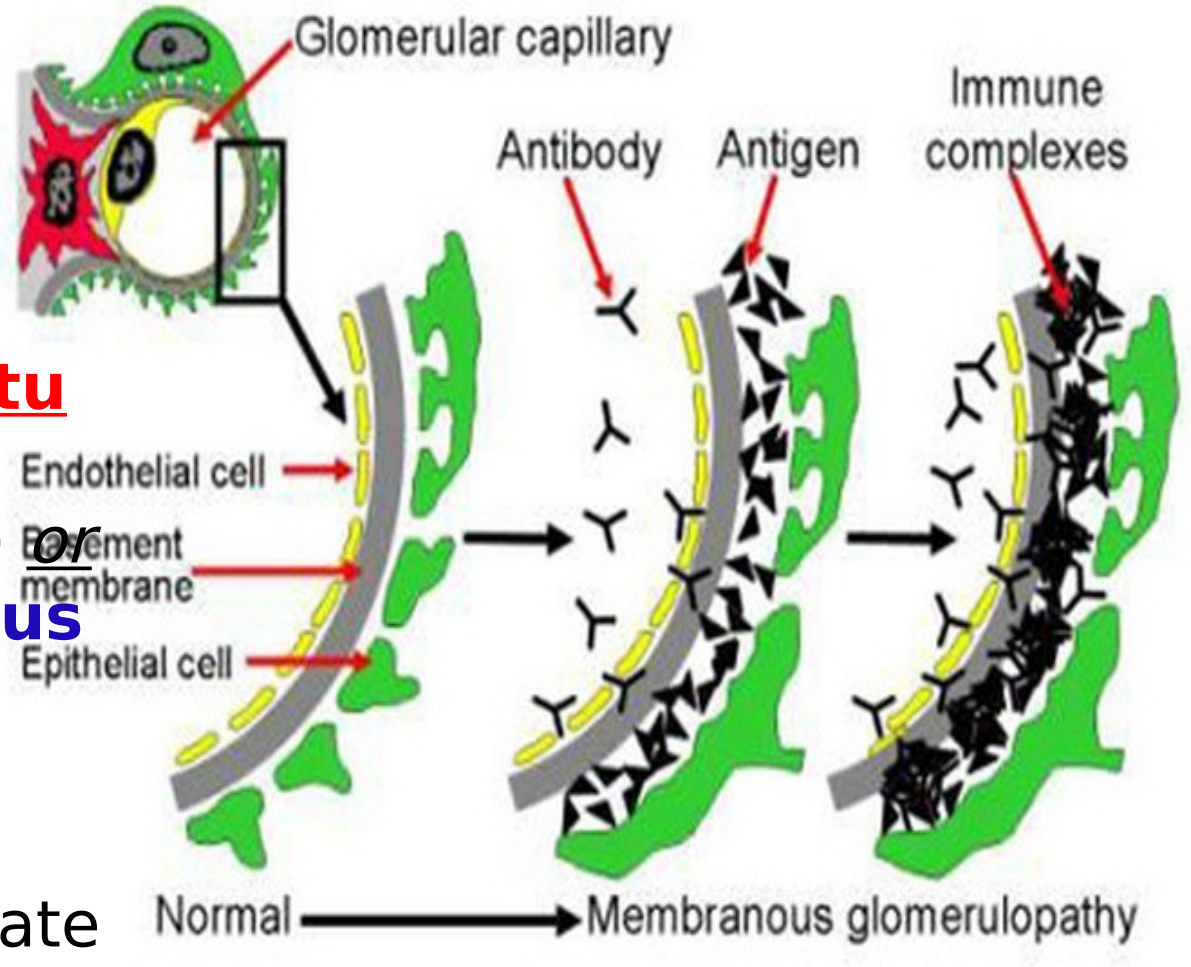
-Podocyte antigens (primary GN) *or*

-Planted antigen in the glomerulus

(Secondary GN in Hepatitis B, Bilharziasis, SLE)

- Antigen-antibody complexes activate complement which damages podocytes

→ proteinuria

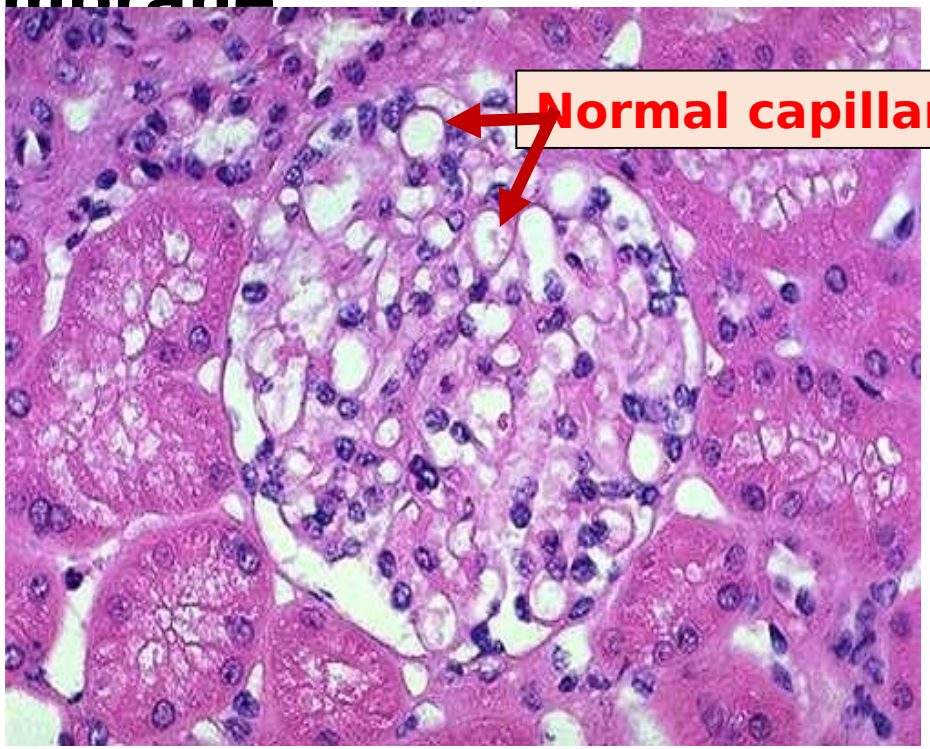


https://www.slideshare.net/drmohammadmanzoor/membranous-glomerulonephritis

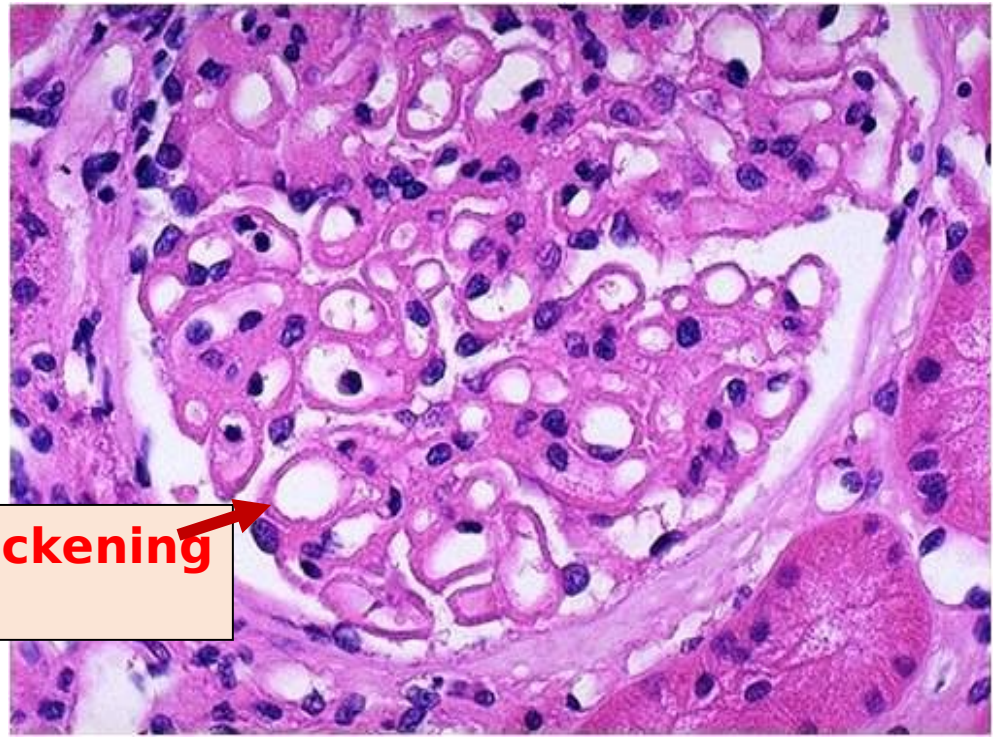
2. Membranous glomerulonephritis (MGN)

Pathological features of glomeruli:

Light microscopy: Diffuse thickening of glomerular capillary basement **membrane**



Normal glomerulus



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2. Membranous glomerulonephritis (MGN)

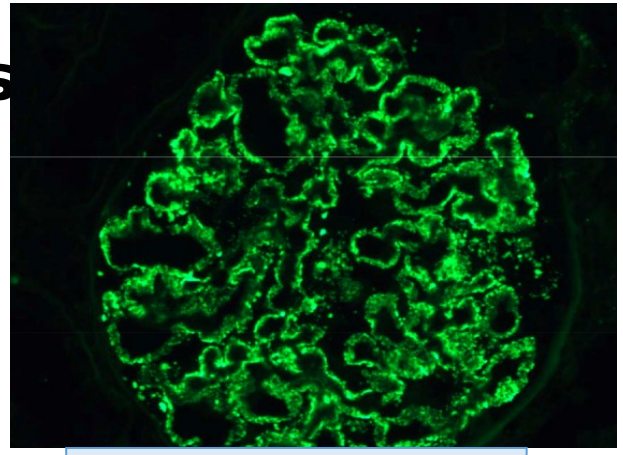
Electron microscopy:

- **Effacement of foot processes** of podocytes
- **Sub-epithelial deposits** separated by outward protrusions of GBM "spikes" (**comb appearance**)

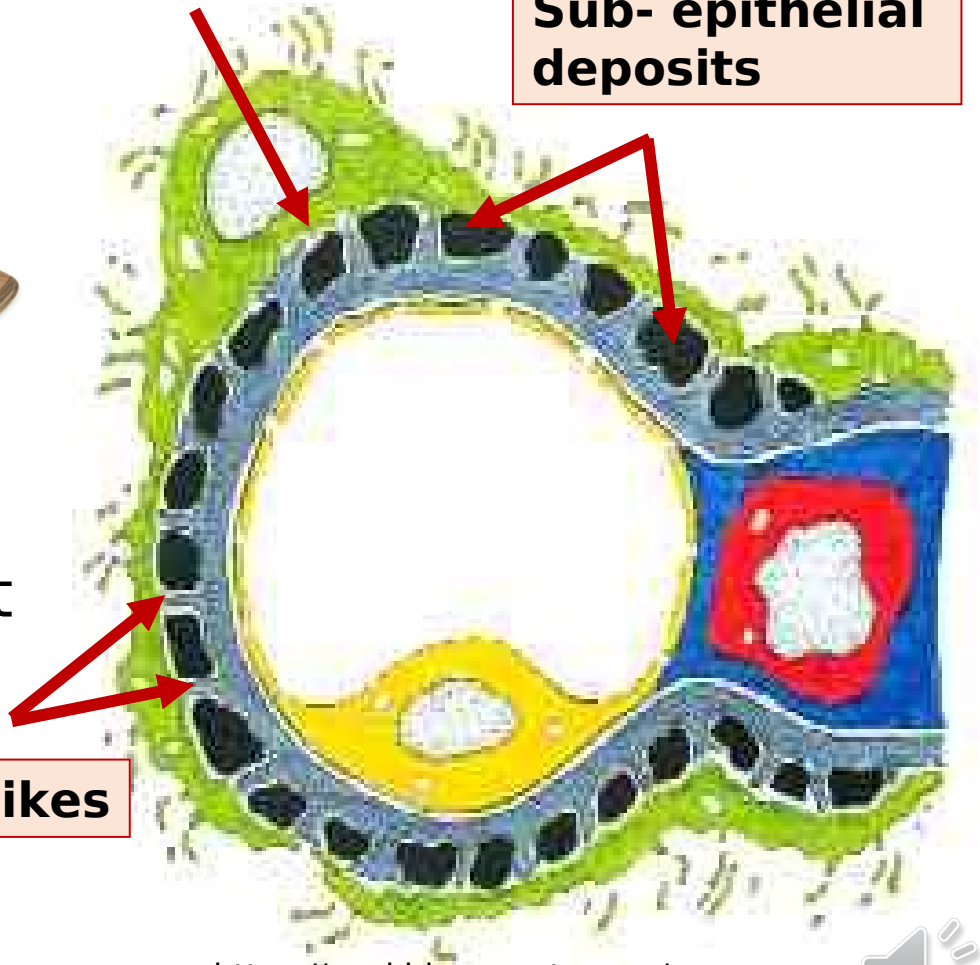
Immunofluorescence:

- **Granular deposits** ent

Fate: Chronic renal failure



Granular deposits



https://www.slideshare.net/drmohammadmanzoor/membranous-glomerulonephritis

https://unckidneycenter.org/kidneyhealthlibrary/glomerular-disease/membranous-nephropathy/

3. Membrano-proliferative glomerulonephritis (MPGN)

This occurs in all ages, particularly late childhood.

Pathogenesis:

✪Type I MPGN (more common)

May be caused by **circulating or insitu** immune complexes.

- ❑ **Primary:**
  The antigen involved is not known.
- ❑ **Secondary:**
  Associated with hepatitis B viral infection, Systemic lupus erythematosus (SLE)

✪Type II MPGN (dense deposit disease)

- ❑Due to presence of autoantibody against **C3 convertase**, called **C3 nephritic factor**, that stabilizes the enzyme and lead to **uncontrolled cleavage of C3** and **excessive activation of the alternative complement pathway**
- ❑ Glomerular capillary basement membrane shows → dense deposits of complement.

3. Membrano-proliferative glomerulonephritis (MPGN)

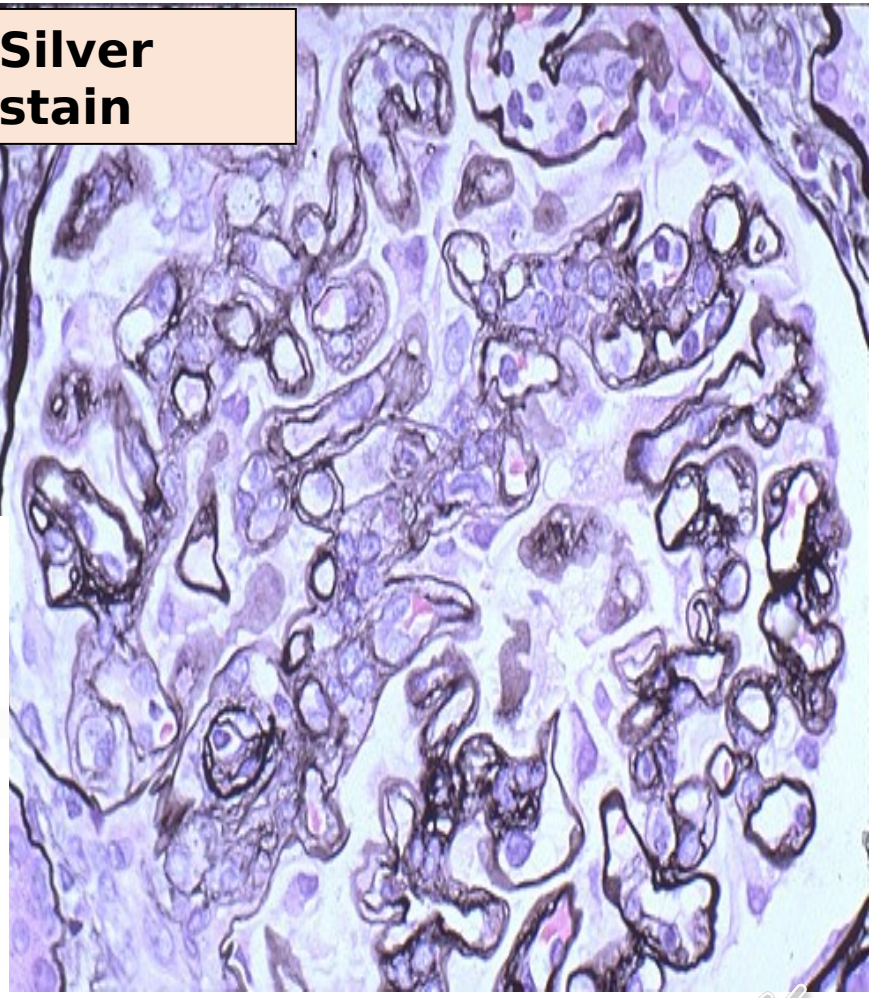
Pathological features of glomeruli

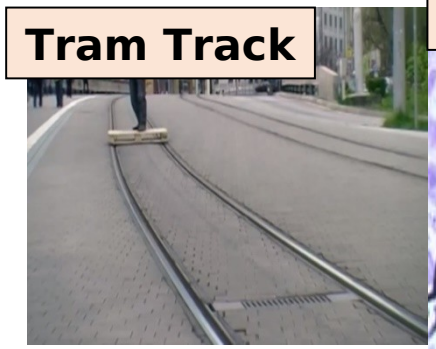
Light microscopy:

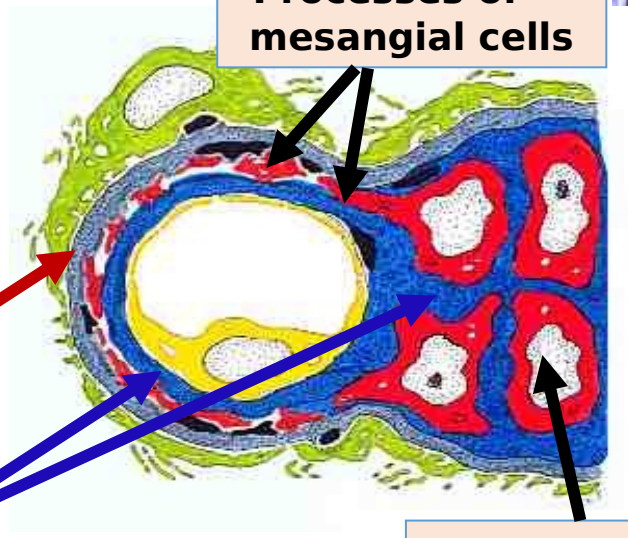
The glomeruli are large showing:

- Proliferation of mesangial cells & endothelial cells.
- Increased mesangial matrix.
- Thickening of capillary basement membrane which appear double contoured **"Tram Track"**

Enlarged glomerulus







https://webpath.med.utah.edu/RENAHTML/RENAL160.html

3. Membrano-proliferative glomerulonephritis (MPGN)

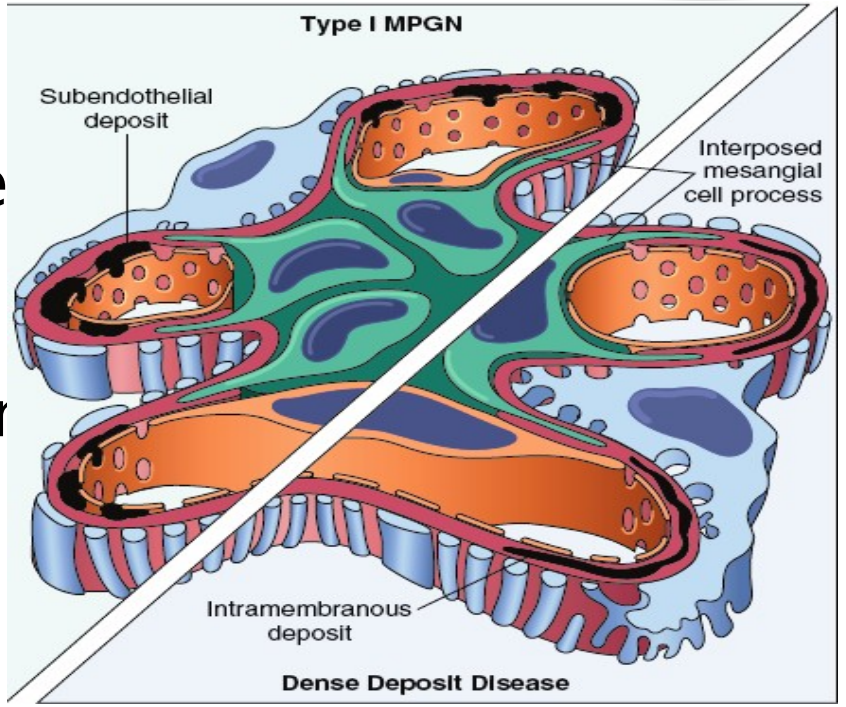
Electron microscopy:

Type I MPGN:

Subendothelial deposits of IgG, IgM & compleme

Type II MPGN:

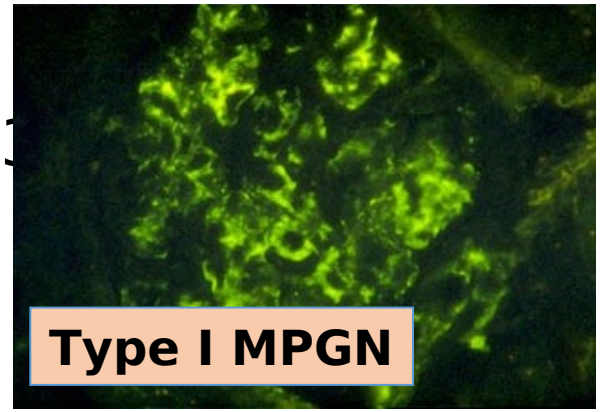
Intra-membranous dense deposits of complemer

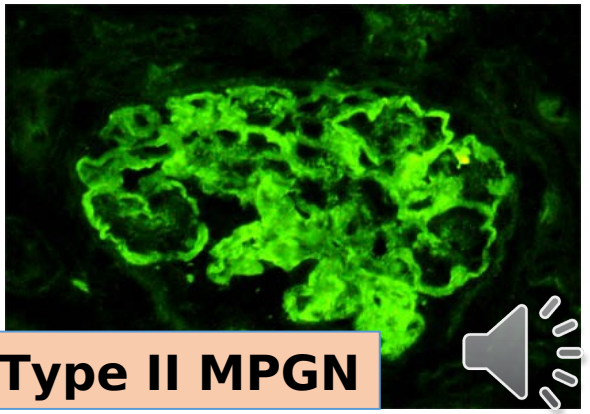


Immunofluorescence:

Type I MPGN: ***granular*** deposits of IgG, IgM & complement

Type II MPGN: ***linear deposits*** of C





Clinical picture :

Nephrotic or nephritic Syndrome

Fate: Chronic renal failure

Quiz

Question 1

Which of the following is a microscopic picture of minimal change GN?

a) Endothelial cell proliferation b) Thickening of the GBM c) Effacement of foot processes c) Mesangial cell proliferation

Question 2

Which of the following is a characteristic feature of nephrotic syndrome ?

a)Heavy protienuria b) hypertension c) Red Cell casts d) Leucocytic casts

Question 3

Which of the following is a microscopic picture of Membranous GN?

Quiz

Question 1

Which of the following is a microscopic picture of minimal change GN?

a) Endothelial cell proliferation b) Thickening of the GBM

c) Effacement of foot processes

c) Mesangial cell proliferation

Question 2

Which of the following is a characteristic feature of nephrotic syndrome ?

a)Heavy protienuria b) hypertension

c) Red Cell casts d) Leucocytic casts

Question 3

Which of the following is a microscopic picture of Membranous GN?

SUGGESTED TEXTBOOKS

1. Robbins basic pathology 10th edition, 2018.Chapter 14: Kidney and its collecting system.

2. Kaplan step 1 pathology lecture notes. Chapter 15: Renal pathology, 2017 (P.143-156)

Thank you